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ORIGINAL ARTICLES

HIV-1 seroconversion incidence following pregnancy and delivery among women seronegative at recruitment in Harare, Zimbabwe

*MT MBIZVO, *J KASULE, *K MAHOMED, **K NATHOO

Abstract

Objective: To estimate the incidence of HIV seroconversion among women following pregnancy and delivery.

Design: A prospective cohort of women who were HIV negative at recruitment on first *antenatal* care visit.

Materials and Methods: Pregnant women were invited to undergo voluntary confidential HIV counselling and blood draw for HIV testing during the first *antenatal* care visit as part of a prospective study of mother-to-child transmission of HIV-1. Repeat tests were conducted at delivery, six weeks *post partum* and at three monthly intervals until 24 months or on termination due to subsequent pregnancy, death or loss to follow up. Logistic regression modelling was used to determine independent predictors of HIV seroconversion.

Results: Among 372 HIV negative pregnant women who were enrolled, 66 seroconverted during follow up, resulting in a sero-incidence of 4.8 per 100 person years (95% confidence interval [CI], 3.1 to 6.5). Women who did not seroconvert during the time of pregnancy or follow up were significantly more likely to have used a condom with their partners (OR = 0.68, 95% CI = 0.47 to 0.99). Women aged 17 years and below had the highest seroconversion incidence (6.25%) followed by those aged 18 to 19 years (5.42%). Women who seroconverted and those who were HIV positive at recruitment were more likely to be married. Lack of education by the partner of a pregnant woman constituted a significant risk factor for HIV seroconversion (OR = 2.8; 95% CI = 1.1 to 11.0).

Conclusions: There is a high HIV seroconversion incidence among women during pregnancy and following delivery, especially those aged 19 years and below. Being married does not protect the women from the risk of HIV seroconversion. Strategies for HIV prevention should target pregnant women and their partners.

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Introduction

Whereas HIV infection rates have plateaued in most developed countries, sub-Saharan Africa continues to experience a high infection rate from heterosexual transmission. It is estimated that 70% of the world's 33

million infected people live in Africa.¹ The high prevalence constitutes a major public health problem which is likely to continue to draw on scarce health resources in the region.

In 1999, it was estimated that 600 000 children worldwide became infected with HIV through mother-to-child transmission (MTCT).² Over 90% of such infections occur

*Department of Obstetrics and Gynaecology
University of Zimbabwe Medical School

**Department of Paediatrics Medical School
P O Box A178
Avondale
Harare
Zimbabwe

Correspondence to:
Professor Michael T Mbizvo
Department of Reproductive Health and Research
World Health Organization
CH211 Geneva 27
Switzerland
E-mail mbizvom@who.ch
Fax: 41-22-791-4171
Tel: 41-22-791-4245

in the resource-poor world, where a median survival of four to five years is found among HIV infected children.³ The majority of mothers in these developing countries (over 95%), breastfeed their children⁴ and the potential for MTCT is a recent cause for concern among policy-makers, programme managers, service providers and researchers.

Transmission of HIV can occur *in-utero*, during labour and delivery or in the *post partum* period through breast milk. Factors influencing the risk of transmission from mother to child include the viral load, genotype and phenotype, strain diversity, the immunological status of the mother, duration of ruptured membranes, mode of delivery and breastfeeding. The risk of HIV infection to the child through breastfeeding could be increased in instances where the mother is infected during pregnancy or during the course of breastfeeding.

In Zimbabwe, whereas the seroprevalence of HIV in pregnant women of up to 30.2% has been documented,⁵ there is no data published on seroconversion among women during pregnancy or following delivery. Amongst male factory workers, a seroconversion incidence of 2.96% (95% CI = 2.47 to 3.52) was reported in Harare.⁶ As MTCT of HIV is an increasingly important public health problem, the present study sought to determine, among other things, risk factors associated with HIV seroconversion during pregnancy and following delivery and its incidence. Such data should help to deal effectively and rationally with counselling and prevention of paediatric HIV infection.

Materials and Methods

Approval for the study was obtained from the Medical Research Council of Zimbabwe, the Medical Superintendent of Harare Central Hospital and the Director of Harare City Medical Services. HIV seropositive and seronegative mothers were identified in early pregnancy following voluntary testing of HIV and counselling in four *antenatal* care clinics of Harare, Zimbabwe. The pregnant women were informed about the optional HIV testing and participation in the project according to guidelines given by the World Health Organization's Special Programme for Research, Research Training and Development (WHO/HRP) which supported the study from 1991 to 1995. Women were invited to participate at their first *antenatal* care visit, during which an interview solicited data on age, parity and area of residence and other socio-demographic characteristics in order to get baseline data on the population under study.

Women testing HIV ELISA positive according to two tests on different blood samples (EIA product 96040, 96043, 6055 Cambridge Biosciences, Ireland) or Western Blot confirmation (product 80486, Cambridge Biosciences or Ancoscreen, Ireland) of discrepant ELISA results, were invited to participate as index subjects. For each enrolled HIV positive woman, an HIV negative pregnant woman in the same five year (quinquennial <20, 20 to 24, 25 to 29 . . .) age interval was selected at random and invited to

serve as a referent or comparison subject. This resulted in a cohort of HIV positive and negative women which was 1:1 distributed within each age category.

During pregnancy and follow up, medical examination was conducted on both women who had tested HIV positive and those testing HIV negative at enrolment.

All women were interviewed at recruitment and underwent a physical examination following blood collection at baseline, 32 and 36 weeks gestation. Further clinical data and blood samples were collected for both mothers and their infants at delivery, at six weeks *post partum* and at three monthly intervals thereafter, until 24 months or on termination due to subsequent pregnancy, death or loss to follow up.

All data were entered in duplicate in precoded forms and checked for computerized data entry. The main study endpoints discussed in this paper were conversion to HIV seropositive status by women testing negative at recruitment, and associated factors. Logistic regression analysis was used to adjust for confounding factors and to elucidate the independent factors associated with HIV seroconversion, including the relative importance of different risk factors.

Results

In the cohort of 758 women followed up, 386 were HIV positive and 372 were seronegative. Of the 372 HIV negative women, 66 seroconverted during follow up, yielding an overall HIV seroconversion incidence of 4.8 per 100 person years (95% CI = 3.1 to 6.5). Table I outlines the HIV seroconversion incidence of the women during follow up.

Table I: HIV seroconversion incidence at delivery and post delivery follow up intervals among women negative at enrolment.

Pregnancy Interval	Seroconversion (n)	HIV incidence per 100 person years
Up to delivery	16	4.32
6 months after delivery	23	4.44
7-12 months	11	5.24
13-24 months	16	5.80
Overall incidence	66	4.80

The women aged 17 years and below had the highest seroconversion incidence (6.25%) followed by those in the 18 to 19 year age group (5.42%). The HIV seroconversion incidence among the women distributed by age is shown in Table II.

Regarding the socio-demographic status of the women, the majority of women who seroconverted (93.9%) and those testing negative at recruitment (98.4%), were married. Among the 386 HIV positive women at recruitment, 94.3% reported that they were married. Being single, separated or divorced did not constitute a risk factor for HIV seroconversion among the women, albeit, their proportion

Table II: HIV seroconversion incidence distributed by age among women negative at enrolment.

Age Group (Years)	Seroconversion (n)		HIV incidence per 100 person years
	N	%	
Overall	66	100	4.80
≤17	5	7.6	6.25
18-19	7	10.6	5.42
20-21	10	15.2	4.88
22-23	8	12.1	4.47
24-25	10	15.2	4.11
26-27	5	7.6	3.76
28-29	6	9.1	3.53
30-34	5	7.6	3.21
35-39	1	1.5	2.7
≥40	1	1.5	2.38

was small. Use of condoms during the time of pregnancy and follow up conferred significant independent protection (in multivariate analysis) against HIV seroconversion (OR 0.68, 95% CI = 0.47 to 0.99).

The largest proportion of women in all the groups were educated to secondary level or above. Lack of education or its level did not constitute a risk factor for HIV seroconversion (odds ratio [OR] = 1.2; 95% CI = 0.6 to 2.3). Seventy four percent of women in the seroconversion and 78% in the seronegative groups had education up to secondary level or above, and in their partners it was 74.2% and 79% respectively. Lack of education in the partners of pregnant women constituted a significant risk factor (OR = 2.8; 95% CI = 1.1 to 11.0) for HIV seroconversion. Occupation of self and partner did not constitute a risk factor for HIV seroconversion.

Medical factors during follow up which were independently associated with the likelihood of seroconversion were: reported urinary tract infection; recent upper respiratory tract infection (URTI) and history of unexplained diarrhoea, as shown in Table III.

Table III: Multivariate analysis of independent risk factors of HIV seroconversion.

Risk Factors	Odds ratio (95%CI)	p value
Urinary tract infection	0.63 (0.4-0.99)	0.04
Recurrent URTI	0.46 (0.22-0.95)	0.03
Unexplained diarrhoea	0.21 (0.05-0.99)	0.04

Medical conditions were similarly distributed and, although present, they were not significantly high during pregnancy and follow up in the women who seroconverted, e.g. groin lymph glands (OR = 0.45; 95% CI = 0.8 to 1.8), axilla lymph glands (OR = 2.2; 95% CI = 0.8 to 6.4), vaginal candidiasis (OR = 0.78; 95% CI = 0.01 to 27.7), oral ulceration (OR = 0.7; 95% CI = 0.02 to 18.2) and oral thrush (OR = 1.4; 95% CI = 0.25 to 7.45).

Discussion

The present findings demonstrate a high risk of HIV acquisition by women during and following pregnancy.

The HIV seroconversion incidence of 4.8 % per year reported is higher than that of 2.9% reported among male factory workers in Harare⁷ during the study period. (However, the prevalence of HIV in both groups was comparable, being 18.0 % in pregnant women⁸ and 19.1% in male factory workers⁹). Independent risk factors for seroconversion among men in the factory worker study were history of a genital ulcer, number of sexual partners and being married but residing separately from the wife. In the present study, the majority of the women were married and there were no behavioural independent risk factors for seroconversion.

The findings point to the need for the promotion of strategies for HIV prevention among pregnant women and those that target their male partners. A most likely scenario is that there is sexual abstinence during pregnancy and following delivery by a large proportion of married women, during which their male partners are exposed to the risk of HIV infection through other relationships. The HIV sero-incidence in this group of women, which is nearly double that of male factory workers, makes it an important target group for innovative HIV prevention strategies. Their HIV infection has prognostic significance to both the mothers themselves and their infants who are likely to get infected through breastfeeding. The *post partum* period might be a high risk and vulnerable period for the acquisition of HIV by women because of mucosal frailty and hormonal changes during this time. A population-based sero-incidence study among women in the reproductive ages in Kigali, Rwanda,¹⁰ established a sero-incidence density of 3.5 per 100 women years over a three year period, with the highest incidence of 7.6 per 100 women years during the first six months *post partum* highlighting also the vulnerability of this group of women.

Approaches which can be considered for HIV prevention in this group include the promotion of mutual abstinence if it is considered acceptable or necessary for the woman to abstain, use of condoms if engaged in other relationships and engaging in other safe sex practices, among male partners of women presenting for *antenatal* care.

In recognition of their vulnerability, women in commercial sex work have been targeted by many AIDS prevention programmes. Such programmes raise awareness of HIV and enable some women to protect themselves through condom use or abstinence from sex. However, such programmes have little impact on the vulnerability of women who are not traditionally considered at risk of HIV, such as pregnant women, especially when they are married.

The present findings demonstrate that pregnancy is one of the major circumstances during or following which women are likely to acquire HIV infection. Thus pregnancy could serve as an entry point for positive male involvement in reproductive health promotion. Policy-makers and reproductive health programme managers are challenged to develop strategies which integrate male partners of pregnant women into HIV prevention programmes. Such targeted programmes could include information, education

and communication (IEC) on family planning choices, possible consequences of sexually transmitted infections (STI) on pregnancy outcome, such as syphilis to the infant and the risk of HIV to father, mother and infant. Although men are known to be concerned with the well being of their partners during pregnancy, they are particularly sensitive to the need to protect their offspring from preventable adverse health outcomes. Thus the *antenatal* care period could present a window of opportunity for reaching men with information aimed at having them identify with and relate to women's reproductive health needs.

The HIV prevalence in pregnant women in the same clinical setting in Harare showed an increase from 18% in 1990⁸ to 30.4% in 1995.⁵ A study conducted in 1999,¹¹ established that the prevalence had plateaued with a seroprevalence of 31.1% detected in the same setting. These data suggest a high HIV infection rate in the sexually active urban population of Zimbabwe. More effective use of clinical care settings to promote HIV prevention may help slow the population spread of HIV.

Independent risk factors for seroconversion among men in the factory worker study were history of a genital ulcer, number of sexual partners and being married but residing separately from one's wife. Thus, health education campaigns should address factors associated with the continued acquisition of HIV in these vulnerable populations.

Information about the timing of HIV-1 transmission from mother to child through breastfeeding is still sparse. Women who seroconvert during pregnancy and following delivery could contribute, to a significant degree, to child seroconversion during the breastfeeding period, thereby contributing to high infant mortality attributable to HIV. Increases in infant mortality due to HIV infection continue to reverse many of the gains in child survival achieved in recent decades through the expanded immunization programme (EPI). The present findings underscore the need to broaden approaches towards HIV prevention and to respond to the health needs of women who traditionally may not have been considered at risk for HIV infection.

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